Intrathecal baclofen for spasticity of spinal origin: seven years of experience

RICHARD D. PENN, M.D.
Department of Neurosurgery, Rush Medical College, Chicago, Illinois

A total of 66 consecutive patients with severe spasticity of spinal cord origin were screened with intrathecal baclofen, and all but two responded with a two-point decrease in their Ashworth spasticity scale score. Of these, 62 elected to receive chronic intrathecal baclofen administration by means of an implanted delivery system. These patients have been followed for an average of 30 months (the first three for 81 months). Intrathecal baclofen has been well tolerated and all serious side effects were transient and have been managed by dose adjustments. The pump presently available has worked safely; the only problem has been stalling in 7% of these devices. The catheter system has had to be repaired in just over one-half of the patients and is the main cause of interruption of drug delivery. Of the 62 patients implanted, 52 (84%) continue to be treated adequately for spasticity; there are three poor long-term responders, four deaths due to underlying disease, and three whose participation has been voluntarily withdrawn. It is suggested that long-term control of spinal spasticity by intrathecal baclofen can be achieved in most patients.

Key Words • intrathecal drug infusion • baclofen • spasticity • spinal cord injury • multiple sclerosis • implantable pump

Since the first report in 1984 that intrathecal baclofen could eliminate spasticity of spinal cord origin, numerous studies in the United States and Europe have reconfirmed the observation. Investigators have documented not only a marked decrease in abnormal tone and spasms with baclofen use, but also an associated improvement in activities of daily living. Sleep patterns, and bladder function, Electrophysiological studies have shown elimination of abnormal hyperactive reflexes and an unmasking of normal motor function as spasticity is reduced. In reviewing data from the combined studies, a recent United States Food and Drug Administration (FDA) panel voted unanimously to approve baclofen for treatment of spinal spasticity. Barring unanticipated difficulties, physicians will soon be able to use intrathecal baclofen with an implanted programmable pump and catheter system without special permission from the FDA or their institutions' committees on human experimentation.

As intrathecal baclofen progresses from being a successful experiment to an approved treatment method, the risks and benefits of its use need to be detailed so that it can be integrated properly into existing medical and surgical procedures for alleviating spasticity. To this end, the results have been reviewed for all 66 patients with spinal spasticity who have been treated with intrathecal baclofen from the initiation of this protocol at Rush-Presbyterian-St. Luke’s Medical Center. This experience shows that effective therapy can be maintained for almost all of the patients over the long term, but that technological problems, especially with the catheter system, may interrupt drug delivery and must be corrected.

Clinical Material and Methods

Patient Selection

A total of 66 patients with severe spasticity and/or spasms of spinal cord origin (spinal trauma in 32 cases, multiple sclerosis in 33 cases, and lateral sclerosis in one case) who had failed oral antispasmodic drug therapy were screened with intrathecal baclofen. Their average age was 40 years (range 10 to 71 years), average duration of spasticity was 8 years (range 0.3 to 41 years), and all had undergone adequate trials of oral baclofen. The intrathecal baclofen protocol was approved by the Rush Human Investigation Committee and informed consent was obtained from each patient.
Intrathecal baclofen for spasticity

Fig. 1. Graph depicting the duration of treatment with intrathecal baclofen, administered via an implanted drug pump, for 62 patients.

Patient Evaluation

Doses of baclofen, 50 to 100 μg, were given by lumbar puncture to test the patient’s response to intrathecal administration. Changes in spasticity were measured using the Ashworth scale (5 = rigid in extension or flexion; 1 = normal tone) and a spasm scale (4 = > 10 spasms/hr; 0 = no spasms). If the Ashworth or spasms scale scores improved by two or more points, the implantation of a programmable pump and catheter system was offered. The surgical details have been described previously. The implanted patients were evaluated for Ashworth and spasms scale scores at the times of pump refill (3- to 6-week intervals), and drug and device complications were noted as they occurred.

Management of Complications

Side effects attributable to medication were managed by reducing the dosage by 10% to 20% in steps until the side effect cleared. Drug overinfusion resulting in somnolence or coma was dealt with by removing baclofen from the drug pump, admitting the patient to the hospital for observation, and providing respiratory support if necessary until the baclofen cleared the central nervous system (in 24 to 36 hours). Pump or catheter malfunctions were treated by replacing the defective part of the system under local anesthesia. Infections were handled by removing the implanted pump system, administering antibiotic medication, and then replacing the system at a new site.

Drug Delivery System

The first nine pumps implanted were a prototype version, but after two overdoses occurred due to pump failures, a newly designed device was employed.* Likewise a thin-walled catheter prone to kinking was replaced by a thicker-walled subcutaneous catheter connected to a thin-walled intraspinal catheter.*

Results

Preliminary Screening

Among 66 patients screened with intrathecal baclofen, 64 responded with a reduction in Ashworth and/or spasms scale scores of two points or more. One failure was in a 44-year-old patient with lateral sclerosis (progressive spastic paraparesis) of 17 years’ duration. The second failure was in a multiple sclerosis patient with severe fixed contractures in his hips, legs, and ankles. Intrathecal baclofen reduced her muscle tone but the contractures did not change, therefore the patient was not implanted. Two patients with spinal cord injury who did respond to baclofen decided not to have the pump implanted, the first because deafferentation pain was not relieved and the second because functional improvement in the paralysis was not achieved.

Maintenance of Effective Treatment

The average treatment period for the 62 implanted patients has been 30 months, with the longest being 84 months (Fig. 1). The Ashworth and spasms scale scores for these patients are shown in Fig. 2. To obtain this level of spasticity control, the baclofen dosage was increased gradually over the first 2 years, after which the requirement tended to stabilize (Fig. 3). In addition to this slowly developing drug tolerance, five patients needed a more rapid increase in dosage to maintain an adequate therapeutic effect, making refills more frequent. When this occurred, the patients were given low-dose morphine (200 to 1000 μg/day) and intrathecal

* SynchroMed Model 8611 H prototype implantable pump, and Model 8703 spinal catheter manufactured by Medtronic, Inc., Minneapolis, Minnesota.

J. Neurosurg. / Volume 77 / August, 1992 237
baclofen was withdrawn. After 2 to 10 weeks they were restarted on baclofen at approximately one-half of the prior dose with good control of spasticity. With the high baclofen concentrations (2000 µg/cu cm) available in the last several years, the need for such medication “holidays” has decreased and these patients can be maintained on higher doses, up to 1500 µg/day.

Three patients have had recurrence of spasms or rigidity after 2, 3, and 3½ years of successful management, in spite of verified drug delivery to the lumbar space. Two patients with good reduction in spasticity withdrew from the study because they wanted more extension rigidity for standing.

Deaths and Infections

Of the 62 implanted patients, four died while receiving continuous intrathecal baclofen. Deaths were due to progression of their multiple sclerosis in two patients, cardiac arrhythmia in one, and lung cancer in one. No patient died because of baclofen treatment or drug pump implantation. Two clinical infections occurred: one was Klebsiella pneumoniae meningitis 6 weeks after implantation and the other a pocket infection 1 month after implantation. Both were treated successfully with antibiotics and removal of the implanted equipment.

In 1989, a batch of vials of baclofen prepared in our hospital pharmacy was contaminated with bacteria (Pseudomonas paucimobilis) and fungus (Wangiella sp). Cultures of all pump reservoirs revealed 19 that tested positive, but no patient developed a clinical infection with either organism. Four pumps contaminated with Pseudomonas alone were treated by injection of gentamicin into the reservoir. The pumps contaminated by fungus were replaced.

Pump, Catheter, and Procedural Complications

Three of the nine prototype pumps failed to function properly. The two most serious malfunctions produced baclofen overdoses and coma. Six of 82 redesigned pumps have failed; in each case the pump stalled, resulting in cessation of baclofen delivery. Replacement of the pumps restored effective therapy. Six pumps were replaced after an average of 54½ months of use when the internal battery became depleted; the expected battery longevity is from 3 to 5 years.

Catheter complications were frequent with both the prototype thin-walled design and the new thick-walled “kink-resistant” model. No improvement in catheter complications occurred as more surgical experience was gained, and cuts and punctures (five instances), kinks (11), dislodgements (three), disconnections (four), and breaks (two) occurred with unfortunate regularity. In three cases, a change in catheter position or catheter replacement restored effective therapy when other problems in delivery could not be found. In two cases, a fibrous scar occluded the catheter tip. Effective intrathecal therapy was restored in all cases by replacing the catheter.

Five procedural complications occurred. Early in the series, two cerebrospinal fluid seromas developed. When a purse-string suture was used around the catheter as it passed through the lumbosacral fascia, no further seromas occurred. One pump was placed upside-down, and one was implanted too close to the superior iliac crest. A wound dehiscence occurred in a thin patient.

Intrathecal Baclofen Complications

The most frequent side effects of intrathecal baclofen were drowsiness (22 cases), dizziness (10), blurred vision (10), and slurred speech (six). Episodes of nausea, orthostatic hypotension, nystagmus, confusion, memory decrease, or dysmetria were rare (three cases or fewer of each). All of these and other rarer side effects were transient and resolved with a reduction in the baclofen dose. No patient discontinued therapy because of these problems. A 150-µg bolus caused somnolence in one patient, and a 1500- and 4000-µg bolus caused coma in two patients for 24 to 36 hours with respiration rates reduced to 4 to 6 breaths/min, but with no hypotension. The patients recovered and baclofen treatment was restarted when spasticity recurred.

One patient with multiple sclerosis but without prior seizures developed grand mal seizures after several months of intrathecal therapy and has had to be placed on anticonvulsant medications. The only side effect that has continued throughout intrathecal baclofen infusion is a dry mouth. In the five affected patients, dosage reduction did not make a difference.

Discussion

Intrathecal baclofen was able to reduce spasms and spasticity in 97% of patients in this consecutive series. The only failures were in a patient with multiple sclerosis with fixed contractures who could not be adequately assessed and in a patient with progressive lateral sclerosis. This nearly 100% effectiveness is unusual for
Intrathecal baclofen for spasticity

any drug treatment and suggests that the basic mechanism that produces spinal spasticity must involve spinal circuits which are inhibited by γ-aminobutyric acid, agonists, of which baclofen is the prime example. The major practical problem that this therapeutic success poses is how to deliver long-term intrathecal baclofen to patients effectively. The new programmable pump used in this study failed in only 7% of cases, each time by stalling. This compares to a 3% failure rate for the simpler nonprogrammable pump employed by Müller in his study of 211 spasticity patients.

While the pump functions well, the catheter system is not as reliable. Cuts, kinks, breaks, disconnections, and dislodgements caused interruption of drug delivery in one-half of our patients. In a large multicenter study in Germany reported by Müller, 26 dislodgements and three kinks occurred in 211 implants of the Infusaid system. Since his patients have not been followed for as long as ours, this may represent a failure rate somewhat better than or similar to ours. The important point to emphasize is that the catheter problems in our patients could be readily corrected surgically, under local anesthesia, and no patient withdrew from treatment due to catheter complications. When a disruption of baclofen delivery occurs, the pump is checked by its computer, the fluid in the reservoir is measured, x-ray films of the catheter are taken, and if necessary, a 111 study can be performed. 119 Sometimes exploration of the system is necessary to reveal the origin of the problem.

Intrathecal baclofen has been well tolerated by the patients. Transient side effects were reported in 31 patients; the only treatment required was lowering the dosage. Unlike oral administration of baclofen, the therapeutic level is not limited by patient drowsiness. The 4:1 ratio between lumbar and cervical concentrations of baclofen when it is given continuously to the lumbar space may explain this relative lack of central complications.3 Overdosing due to device or human error will result in coma and mild respiratory depression.6,8,10 To date, no patient has been reported to have died from an overdose, and the central effects clear in 24 to 48 hours. For mild overdoses (in the 150- to 800-µg range), physostigmine may be a useful stimulant.10 At present a direct antagonist is not available clinically.

The decision to use this treatment must rest upon several points.20 Have oral antispasmodic medications truly failed? Are their side effects too great? Does the gain in function and comfort by controlling the spasticity justify the invasive procedure and the maintenance of the drug delivery system? Can a single, definitive surgical procedure such as a myelotomy accomplish the same goals?18 Does a patient’s spasticity need to be controlled precisely for functional gains? Once a drug pump treatment is started, it is our experience that the vast majority of patients will insist that it be continued and, with proper management and surgical intervention as necessary, we find that it is possible to do so.

Acknowledgments

I thank Suzanne Savoy, Janet Gianino, and Michelle York who, as nurse practitioners, gave excellent continuing care for the patients, and Rita Hirsch and Scott Ward from Medtronic, Inc., who provided prompt, reliable, and courteous technical support.

Disclosure

The author does not have a financial interest in the instrumentation or methodology reported in this article.

References

16. Penn RD, Kroin JS: Long-term intrathecal baclofen in-


Manuscript received October 15, 1991.
Accepted in final form January 3, 1992.
This work was supported by grants from the National Institutes of Health, the American Paraplegia Association, and the orphan drug division of the FDA.
Address reprint requests to: Richard D. Penn, M.D., Department of Neurosurgery, Rush-Presbyterian-St. Luke’s Medical Center, 1653 West Congress Parkway, Chicago, Illinois 60612.